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10/597,860	08/10/2006	Paul Kenneth Spearing	PU60741	7249

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EXAMINER	
MOORE, SUSANNA	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/597,860	SPEARING, PAUL KENNETH	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/5/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 5/5/2008 is acknowledged. Group I, drawn to thiazolo[3,4-d]pyrimdines and simple compositions, thereof embraced by claims 1-5 was elected by Applicant. Applicant further elected the specie 3-amino-5-butyl-7-cyclopentylisothiazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (Example 1). Applicant has not pointed to any errors in the Examiner's analysis of the classification of the different inventions. The requirement is deemed proper and is therefore made **FINAL**.

There are 6 claims pending and 5 under consideration. Claims 1-4 are compound claims. Claim 5 is a composition claim. Claim 6 is a method of using claims, which is currently withdrawn from consideration. This is the first action on the merits. The application concerns some thiazolo[3,4-d]pyrimidine compounds and simple compositions thereof.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted Thiazolo[3,4-d]pyrimidines as Agonists of the Parathyroid Hormone (PTH) Receptor.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/10/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

This application contains claims 1-6, drawn to an invention nonelected without traverse in the paper of 5/5/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The variables R^1 and R^2 are vague. Said variables are not defined on formula (I). Furthermore, the variables R1 and R2 are defined on formula (I) but are not defined with substituents.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conjugate of claim 1 or pharmaceutically acceptable salts of said conjugate does not reasonably provide enablement for a solvate of a conjugate of claim 1. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention is a conjugate of claim 1, or a pharmaceutically acceptable salt of said conjugate. There is no teaching of solvates of the conjugates of claim 1 in the specification.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound (See Vippagunta, et al.)

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active in vivo. Solvates and hydrates cannot always be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular hydrate or solvate.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention.

The breadth of the claims

The breadth of the claims is a conjugate of claim 1 or a pharmaceutically acceptable salt or solvate thereof.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make solvates of a conjugate of claim 1 it would require undue experimentation to figure out the solvents, temperatures and reaction times that would provide solvates of the above compounds.

To overcome this objection, Applicant should submit an amendment deleting the term "solvates".

Claims 1 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of Formula 1, wherein R^1 and R^2 are C_{1-8} alkyl, C_{2-8} alkylene, C_{3-8} cycloalkyl does not reasonably provide enablement for compounds of Formula 1, wherein R^1 and R^2 are aryl, heteroaryl, heterocycloalkyl, C_{3-6} cycloalkylaryl, or heterocycloaryl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see In re Vaeck, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims: Scope of the compounds. Owing to the range of many variables, millions of substituted thiazolo[3,4-d]pyrimidines are embraced.

(B) The nature of the invention: The invention is a highly substituted thiazolo[3,4-d]pyrimidines.

(C) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(D) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of Formula 1, under Preparation on page 10 of the Specification, but does not show the starting material used to make the variety of compounds claimed. There is limited evidence in the Specification of the example compounds that only cover a small portion of the substituents claimed of Formula 1. Thus, there is no specific direction or guidance regarding said compounds of Formula 1 specifically mentioned in Scope.

The specification does not provide any support for the synthesis of compounds of Formula 1, wherein R^1 and R^2 are aryl, heteroaryl, heterocycloalkyl, C_{3-6} cycloalkylaryl, or heterocycloaryl.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 21'64.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991,169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the

application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

(E) State of the Prior Art: These compounds are substituted thiazolo[3,4-d]pyrimidines of Formula I wherein R^1 and R^2 are C_{1-8} alkyl, C_{2-8} alkylene, C_{3-8} cycloalkyl which are well documented in the art. So far as the examiner is aware, no substituted thiazolo[3,4-d]pyrimidines of Formula I wherein R^1 and R^2 are aryl, heteroaryl, heterocycloalkyl, C_{3-6} cycloalkylaryl, or heterocycloaryl of any kind have been made or used.

(F) Working Examples: Applicant shows examples 1-3 but no working examples were shown of Formula I wherein R^1 and R^2 are aryl, heteroaryl, heterocycloalkyl, C_{3-6} cycloalkylaryl, or heterocycloaryl.

(G) Skill of those in the art: The ordinary artisan is highly skilled.

(H) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted groups on Formula i. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Niess et. al. (DE 2248231).

The reference teaches the compound of formula (I), wherein R^1= butyl, R^2= butyl, A= sulfur and B= nitrogen in ethanol, a pharmaceutically acceptable excipient, see page 9, table 1, compound 6. Note, the reaction at the top of page illustrates the removal of the R^3 group in the reference. Furthermore, Applicant recites ethanol as an acceptable excipient, see page 7, line 3. See also the STN printout with the compound and registry number of said compound. Thus, claims 1-5 are anticipated by Niess et. al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

/Brenda L. Coleman/
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